UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,567	11/13/2001	Christel Schmelzer	1/1171	7734

28501 7590 03/30/2006

MICHAEL P. MORRIS
BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER
CHONG, YONG SOO

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,567	SCHMELZER ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-11 and 28-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-11 and 28-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 1/20/2006. Claims 5-6, 12-27 have been cancelled. Claim 1 has been amended. Claims 1-4, 7-11, 28-46 are pending and are examined herein. Applicant's arguments have been fully considered but found persuasive to withdraw the objection and double patenting rejections over US Patents 6,630,466; 6,680,345; 6,919,325 only. The remaining rejections are the provisional obviousness-type double patenting rejection over Application No. 10/736,264 and the USC 103(a) rejection, which are maintained for reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 7-11, 28-46 are rejected under 35 U.S.C. 103(a) as being obvious over Freund et al. (WO 97/01329 in German, equivalent to US Patent 6,491,897, PTO-892) in view of Hochrainer et al. and Wolf et al. (of record).

Freund et al. discloses a propellant free pharmaceutical composition comprising the active agents or combinations of active agents including tiotropium bromide and salmeterol (see 6,491,897, the title, abstract, col.1 line 66 to col. 2 line 15, especially col.2 line 5, 8, 15), which is in a form suitable for inhalation administration, i.e. use in nebulizers (see abstract and col.2 line 1). The pharmaceutical composition of Freund et al. comprises acids such as hydrochloride acid, sulphuric acid, phosphoric acid (see col.2 line 60-64) which form a pharmaceutically acceptable salts with the active agents, and also comprises adjuvant (see col. 5 line 14-15), and water and ethanol (see col.1 line 40-48) wherein the pH of the solution is in the range of 2-7, especially 3-4 or 3.2-4.5 within the instantly claimed range (see col.2 line 66-67,. claim 2-3), and cosolvent such as isopropyl alcohol, polypropylene glycol, glycol ether (see col.1 line 51-58), and flavoring and ascorbic acid and other adjuvants (see col.2 line 62-64). The propellant free pharmaceutical composition therein is useful in a method of treating obstructive lung diseases such as asthma (see col.1 line 11-15).

Freund et al. does not expressly exemplify the particular combination composition of tiotropium bromide and salmeterol. Freund et al. does not expressly disclose the effective amounts of tiotropium bromide and salmeterol in the composition herein to be administered. Freund et al. does not does not expressly disclose the compositions therein contained in single preparation or two separate

preparations.

Hochrainer et al. and Wolf et al. teach the claimed tiotropium and salmeterol respectively as old and well known in combination with various pharmaceutical carriers and excipients in both a powder and liquid form useful for atomization. Hochrainer et al. teach tiotropium and other asthma, and COPD medicaments in combination with polyalcohols, (page 5), EDTA (page 5, line 26), benzalkonium chloride (page 5, line 66), vitamin C (page 4, line 58). These compositions are taught in the particle size range (970) page 5, line 10-15), pH (970) page 4, line 60-62) and encapsulation schema herein envisioned. These pharmaceutical formulations are taught as useful for treating COPD and asthma, viewed by the skilled artisan as indistinguishable from that use herein claimed.

It would have been obvious to a person of ordinary skill in the ad at the time the invention was made to employ the particular combination composition of tiotropium bromide and salmeterol, and to optimize the effective amounts of active agents in the composition herein to be administered, and to store the combination in a single or two separate containers.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular combination composition of tiotropium bromide and salmeterol, since the combinations of active agents including tiotropium bromide and salmeterol in a propellant free pharmaceutical composition is disclosed by Freund et al. Thus, any combinations of active agents including tiotropium bromide and salmeterol disclosed by Freund et al. would have had the reasonable expectation of

success as used in a propellant free pharmaceutical composition for treating obstructive lung diseases such as asthma.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because tiotropium and salmeterol respectively are old and well known to be used in treating COPD and asthma according to Hochrainer et al and Wolf et al. Thus, the optimization of the known amounts of the known active agents to be administered is considered well within the skill of artisan.

Moreover, one of ordinary skill in the art would have reasonably expected that combining tiotropium and salmeterol both known useful for the same purpose, i.e., treating COPD and asthma, would improve the therapeutic effects for treating the same diseases, and/or would produce additive therapeutic effects in treating the same.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose, the idea of combining them flows logically from their having been individually taught in prior art.

See In re Kerkhoven, 205 USPQ 1069, CCPA 1980.

Further, the patient pack, e.g., a single or two separate containers, is all deemed obvious since they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Thus the claimed invention as a whole is clearly prima facie obvious over the

combined teachings of the prior art.

Response to Argument

Applicant's arguments and the declaration of Alexander Walland, under 37 CFR 1.132, filed June 6, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant's argue that (the Examiner fails to provide a specific teaching in either Hochrainer or Wolf to the claimed combination and there is no teaching, suggestion, or incentive in Hochrainer or Wolf to modify the singly specifically exemplified composition containing the combination claimed herein.

Applicant's arguments are not found persuasive. In this case, the primary reference cited herein, Freund et al. discloses a propellant free pharmaceutical composition comprising the active agents or combinations of active agents including tiotropium bromide and salmeterol, which is in a form suitable for inhalation administration, i.e. use in nebulizers (see abstract and col.2 line 1). The pharmaceutical composition of Freund et al. comprises acids such as hydrochloride acid, sulphuric acid, phosphoric acid which form a pharmaceutically acceptable salts with the active agents, and also comprises adjuvant (see col. 5 line 14-15), and water and ethanol (see col.1 line 40-48) wherein the pH of the solution is in the range of 2-7, especially 3-4 or 3.2-4.5 within the instantly claimed range, and cosolvent such as isopropyl alcohol, polypropylene glycol, glycol ether, and flavoring and ascorbic acid and other adjuvants. The propellant free pharmaceutical composition therein is useful in a method of treating

obstructive lung diseases such as asthma, as instantly claimed.

Thus, any combinations of active agents including tiotropium bromide and salmeterol disclosed by Freund et al. would have had the reasonable expectation of success as used in a propellant free pharmaceutical composition for treating obstructive lung diseases such as asthma.

Therefore, the disclosure of Freund et al. has clearly provided the motivation to make the present invention, a propellant free pharmaceutical composition comprising tiotropium and salmeterol or their salts.

Moreover, Hochrainer et al. and Wolf et al. have been cited by the examiner primarily for its teaching that the claimed tiotropium and salmeterol respectively as old and well known in combination with various pharmaceutical carriers and excipients in both a powder and liquid form useful for atomization and in methods for treating asthma, and COPD.

Thus, the claimed invention is clearly obvious in view of the prior art.

Further, Applicant's declaration (of Alexander Walland) under 37 CFR 1.132, is insufficient to overcome the 103(a) rejection herein. The testing results in the declaration merely show that a single combination of tiotropium bromide in 3 μg and salmeterol hemisulfate in 6 μg or 12 μg. Note that unexpected results to rebut the prima facie case, the scope of the showing must be commensurate with the scope of the claims. In re Coleman 205 USPQ 1172, In re Greenfield, 197 USPQ 227, In re Lindener, 173 USPQ 356., In re Payne, 203 USPQ 245. In the instant case, the evidence in the examples herein is also not commensurate in scope with the claimed

invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed composition, and in the claimed range of the ratio of tiotropium and salmeterol. See MPEP 716.02(d).

Therefore, the evidence presented in Applicant's declaration herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SHENGJUN WANG
PRIMARY EXAMINER